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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/709,572	05/14/2004	Itzhak Bentwich	050992.0202.01USCP	3571

37808 7590 10/15/2009

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KANSAS CITY, MO 64112

EXAMINER	
WOLLENBERGER, LOUIS V	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
10/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/709,572	BENTWICH ET AL.	
	Examiner	Art Unit	
	Louis Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26,29,30 and 35-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,29,35 and 37* is/are rejected.

7)☒ Claim(s) *26,30,36 and 38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/21/2009 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 8/21/2009 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 5/21/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 8/21/2009, claims 25, 26, 29, 30, and 35-38 are pending and examined herein.

The indicated allowability of claims 25 and 29 is withdrawn in view of the newly discovered reference(s), cited below, and upon further consideration of the claims under 35 USC 112, first paragraph (written description).

Election/Restrictions

In the reply filed 2/25/08, Applicant elected, without traverse, SEQ ID NO:159.

Applicant's previous amendment to claim 30, deleting references to all previously recited SEQ ID NOs except SEQ ID NO:6821380 was considered to represent constructive election of SEQ ID NO:6821380.

Specification

Applicant's 8/21/2009 amendment to the specification so as to be in harmony with the claims pursuant to MPEP § 1302.01 and under 37 CFR 1.52(e)(5) to amend the specification to include in the paper portion of the specification all descriptive matter pertinent to SEQ ID NO:159 and 6821380 that was previously submitted in tables on compact disc, is acknowledged. The amendment has been entered into the application.

Upon review of the 22-page amendment filed 8/21/2009, it would appear that some nucleotide sequences shown therein are not identified by SEQ ID NO: identifier. See for example page 13, bottom, and page 12. Applicant is respectfully requested to review the amendment to ensure the application as amended complies with 37CFR 1.821-1.825 and that each sequence shown therein is clearly identified by a SEQ ID NO: identifier and is also disclosed in the sequence listing as required by the Sequence Rules.

Claim Rejections - 35 USC § 112, second paragraph—withdrawn

The rejection of Claims 35-38 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicant's amendment to the claims, filed 8/21/2009.

Claim Rejections - 35 USC § 112, first paragraph (new matter)—withdrawn

The rejection of Claims 35-38 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicant's amendment to the claims, filed 8/21/2009.

Claim Objections

Claim 29 is objected to because of the wording in part (c), reciting "80% nucleotides identical to..."

Claims 26 and 30 are objected to because of the language "is of the sequence," since it is unclear whether the language is intended to broaden the claim beyond the sequence consisting of SEQ ID NO:159 or 6821380, and since it is redundant. Amending the claims to recite "wherein the sequence is SEQ ID NO:159" or "is SEQ ID NO:6821380" would be remedial. Claims 36 and 38 are objected to therefor.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. As Applicant is aware, to obtain the benefit of a prior-filed application, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Currently, Applicant claims benefit to the following applications:

** CONTINUING DATA *********************
This application is a CIP of 10/707,975 01/29/2004 ABN
and is a CIP of 10/707,980 01/29/2004
and is a CIP of 10/707,147 11/24/2003
and is a CIP of 10/604,985 08/29/2003 ABN
and is a CIP of 10/651,227 ABN
and is a CIP of 10/649,653 ABN
and is a CIP of 10/604,926 08/27/2003 ABN
and is a CIP of 10/604,726 08/13/2003
and is a CIP of 10/604,727 08/13/2003 ABN
and is a CIP of 10/708,204 02/16/2004
and is a CIP of 10/708,953 04/02/2004
and claims benefit of 60/521,433 04/26/2004
** FOREIGN APPLICATIONS *********************
ISRAEL PCT/IL03/00998 11/26/2003

With the exception of 10/708953, written description support is not found in any of the prior filed applications for SEQ ID NO:159 or 6821380 (exemplary alignments below). Should applicant disagree, Applicant is invited to point out with particularity, by page and line number, where such support may be found.

For purposes of this examination the earliest effective filing date of claims 25, 26, 29, 30, and 35-38 is considered to be that of the instant application: 5/14/2004.

```
RESULT 7
US-10-708-953A-2240402
; Sequence 2240402, Application US/10708953A
; GENERAL INFORMATION:
;  APPLICANT: ROSETTA GENOMICS LTD
;  TITLE OF INVENTION: BIOINFORMATICALLY DETECTABLE GROUP OF NOVEL REGULATORY
;  TITLE OF INVENTION:  OLIGONUCLEOTIDES AND USES THEREOF
;  FILE REFERENCE: 55036
;  CURRENT APPLICATION NUMBER: US/10/708,953A
;  CURRENT FILING DATE:  2004-04-02
;  NUMBER OF SEQ ID NOS: 2254510
;  SOFTWARE: PatentIn version 3.3
; SEQ ID NO 2240402
;   LENGTH: 87
;   TYPE: RNA
;   ORGANISM: Homo sapiens
US-10-708-953A-2240402

  Query Match            100.0%;  Score 87;  DB 50;  Length 87;
  Best Local Similarity   67.8%;
  Matches   59;  Conservative   28;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy          1 TCTCATGCTGTGACTCTCTGGAGGGAAGCACTTTCTGTTGTCTGAAAGAAAACAAAGCGC 60
              :|:||:||:|:|||:|:|:|||||||||||||:::|:|::|:|:||||||||||||||||||
Db          1 UCUCAUGCUGUGACUCUCUGGAGGGAAGCACUUUCUGUUGUCUGAAAGAAAACAAAGCGC 60

Qy         61 TTCTCTTTAGAGTGTTACGGTTTGAGA 87
              ::|:|:::||||:|::||||:::||||
Db         61 UUCUCUUUAGAGUGUUACGGUUUGAGA 87
```

```
RESULT 36
US-10-708-953A-78539
; Sequence 78539, Application US/10708953A
; GENERAL INFORMATION:
;  APPLICANT: ROSETTA GENOMICS LTD
;  TITLE OF INVENTION: BIOINFORMATICALLY DETECTABLE GROUP OF NOVEL REGULATORY
;  TITLE OF INVENTION:  OLIGONUCLEOTIDES AND USES THEREOF
;  FILE REFERENCE: 55036
;  CURRENT APPLICATION NUMBER: US/10/708,953A
;  CURRENT FILING DATE:  2004-04-02
;  NUMBER OF SEQ ID NOS: 2254510
;  SOFTWARE: PatentIn version 3.3
; SEQ ID NO 78539
;   LENGTH: 22
;   TYPE: RNA
;   ORGANISM: Homo sapiens
US-10-708-953A-78539

  Query Match             100.0%;  Score 22;  DB 50;  Length 22;
  Score over Length       100.0%;
  Best Local Similarity   68.2%;
  Matches   15;  Conservative    7;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 ACAAAGCGCTTCTCTTTAGAGT 22
              ||||||||||::|:|:::|||||:
Db          1 ACAAAGCGCUUCUCUUUAGAGU 22
```

Claim Rejections - 35 USC § 112, first paragraph (written description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Upon further consideration, Claims 25, 29, 35, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, complete or partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.

In embodiment (a), Claims 25 and 29 expressly embrace all nucleic acid sequences 19-24 and 50-140 nucleotides in length comprising "at least 19 consecutive nucleotides of SEQ ID NO:159," a bioinformatically predicted, 22-nucleotide mature miRNA, asserted by applicant to be useful for inhibiting the expression of mRNAs from the gene EGFR (page 4 Remarks filed 3/10/09; and see 14 of the amendment to the specification filed 8/21/2009). SEQ ID NO:159 is not 100% complementary to any EGFR sequence or any other mRNA sequence. Thus, these claims embrace a large genus possible nucleic acid sequences, which may be only ~86% identical to SEQ ID NO:159, and whose only common structure is any contiguous 19-nt sequence from SEQ ID NO:159.

In embodiment (c), Claims 25 and 29 are even broader, claiming all nucleic acid sequences 19-24 and 50-140 nucleotides in length that are at least 80% identical to those recited in part (a) or the complements thereof (part (b)). While the Application adequately describes and shows possession of the nucleotide sequences SEQ ID NO:159 and 6821380, the hairpin miRNA precursor from which SEQ ID NO:159 is said to derive, and indicates that such sequences will more likely than not inhibit the expression of a human EGFR gene (NM_005228), the

application does not describe the genus of sequences defined by the claims that have this function or that have any other well established function. A rough calculation suggests that a substantial number of the sequences embraced by parts (c) include sequence that are no more than 69% identical to SEQ ID NO:159; sequences that are 80% identical to sequences that share on 19 of 22 nucleotides in common with SEQ ID NO:159, includes sequences that share between 15-16 nucleotides in common with SEQ ID NO:159.

Thus, the claims are extremely broad. Adequate written description does not exist in the instant application for all these sequences. While Applicant has disclosed the relevant identifying features of SEQ ID NO:159 for performing the function disclosed in the specification, Applicant has not disclosed the identity all sequences of 19, 20, 21, 23, and 24 nucleotides in length that will perform this function. Applicant, for example, has not disclosed which 2-3 nucleotides may be added or subtracted from the sequence while retaining the disclosed activity, nor is there any evidence to show that any 2-3 nucleotides may be added or subtracted while retaining the asserted utility. While applicant describes one sequence of 50-140 nucleotides in length that comprises SEQ ID NO:159 (namely, SEQ ID NO:6821380) that may perform the asserted utility, applicant has not described the countless numbers of other sequences of this length that comprise SEQ ID NO:159, much less that comprise SEQ ID NO:159 and have the function asserted by the application or, for that matter, any other specific function.

While the specification discloses at paragraphs 41 and 42 that a hairpin precursor may be anywhere from 50-140 nucleotides in length and may be processed by a dicer enzyme to yield an oligonucleotide that is 19 to 24 nucleotides in length, these passages simply summarize the possible lengths of miRNAs in a cell and do not reasonably disclose that the miRNA

corresponding to SEQ ID NO:159 or its precursor, SEQ ID NO:6821380, may be of any length in this range, and there is no evidence to show the activity associated with these sequences (i.e., structures) could be extrapolated to any and all nucleotide sequences having only 19 nucleotides of SEQ ID NO:159, much less only 15-16 nucleotides of SEQ ID NO:159. Applicant provides no disclosure showing which nucleotides or at what position nucleotides may be added or subtracted while retaining the activity specific to the invention. In fact the Examiner is unable to find any passage or evidence in the application as filed expressly or impliedly conveying that any consecutive 19-nucleotide sequence of SEQ ID NO:159 may be used to regulate EGFR expression or even to sequence-specifically probe for EGFR. Moreover, Applicant has not disclosed which sequences may be added and where to SEQ ID NO:159 while retaining its specific activity.

Certainly, the application does not disclose by words or any other representation that any 19-24 or 50-140 nucleotide sequence having a mere 69% identity to SEQ ID NO:159 is a part of the invention, as now claimed in part (c) of claims 25 and 29.

Accordingly, only those sequences consisting of, complementary to, and encoded by and equivalent in length to SEQ ID NO:159 and 6821380 are adequately described in the specification.

Applicant is reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25 and 35 are rejected under 35 U.S.C. 102(e) as being anticipated by Khvorova et al. (US 2007/0031844 A1).

Khvorova et al. disclosed functional or hyperfunctional short interfering RNAs of 19-25 bases comprising the 19-nucleotide sequence SEQ ID NO: 1216559, shown below. At paragraph 118 and 293, it is represented that the siRNA may be synthesized as a 21-mer comprising any one of the recommended 19-nt sequences disclosed therein such as SEQ ID NO: 1216559. As shown by the alignment below, the 19-25 base siRNA comprising SEQ ID NO: 1216559 would comprise a sequence within the scope of parts (c) and (d) of claim 25 inasmuch as it would comprise a sequence that is at least 80% identical to a sequence that comprises at least 19-consecutive nucleotides of SEQ ID NO:159, or the complement thereof. At paragraph 277 it is disclosed the strands of the siRNA may be encoded by a vector.

```
RESULT 83
US-10-714-333A-1216559/c
; Sequence 1216559, Application US/10714333A
; Publication No. US20070031844A1
; GENERAL INFORMATION:
;  APPLICANT: Dharmacon, Inc.
;  APPLICANT:  Khvorova, Anastasia
;  APPLICANT:  Reynolds, Angela
;  APPLICANT:  Leake, Devin
```

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;  APPLICANT:  Marshall, William
;  APPLICANT:  Scaringe, Stephen
;  TITLE OF INVENTION: Functional and Hyperfunctional siRNA
;  FILE REFERENCE: 13499US
;  CURRENT APPLICATION NUMBER: US/10/714,333A
;  CURRENT FILING DATE:  2003-11-14
;  PRIOR APPLICATION NUMBER: 60/502,050
;  PRIOR FILING DATE: 2003-09-10
;  PRIOR APPLICATION NUMBER: 60/426,137
;  PRIOR FILING DATE: 2002-11-14
;  NUMBER OF SEQ ID NOS: 1591911
;  SOFTWARE: Proprietary
; SEQ ID NO 1216559
;   LENGTH: 19
;   TYPE: RNA
;   ORGANISM: Homo sapiens
US-10-714-333A-1216559

  Query Match             67.3%;  Score 14.8;  DB 17;  Length 19;
  Score over Length       77.9%;
  Best Local Similarity   88.9%;
  Matches   16;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          2 CAAAGCGCTTCTCTTTAG 19
              ||||  ||||||||||||
Db         18 CAAACTGCTTCTCTTTAG 1
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Claims 29 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Wohlgemuth et al. (US Patent 6,905,827).

As shown by the alignment below, Wohlgemuth et al. disclosed a 50-nucleotide DNA sequence, SEQ ID NO: 2866, that comprises a sequence that is at least 80% identical to the complement of a sequence that comprises at least 19 consecutive nucleotides of SEQ ID NO:159. At column 17, lines 50-61, and elsewhere, vectors for cloning and expressing nucleic acid sequences are also disclosed

```
RESULT 7
US-10-131-827-2866/c
; Sequence 2866, Application US/10131827
; Patent No. 6905827
; GENERAL INFORMATION:
;  APPLICANT: Wohlgemuth, Jay
;  APPLICANT:  Fry, Kirk
;  APPLICANT:  Woodward, Robert
;  APPLICANT:  Ly, Ngoc
;  TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR DIAGNOSING AND MONITORING AUTOIMMUNE AND
;  TITLE OF INVENTION:  CHRONIC INFLAMMATORY DISEASES
;  FILE REFERENCE: 506612000120
;  CURRENT APPLICATION NUMBER: US/10/131,827
;  CURRENT FILING DATE:  2002-09-06
;  PRIOR APPLICATION NUMBER: US 10/006,290
;  PRIOR FILING DATE: 2001-10-22
;  PRIOR APPLICATION NUMBER: US 60/296,764
;  PRIOR FILING DATE: 2001-06-08
;  NUMBER OF SEQ ID NOS: 9090
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 2866
```

```
;   LENGTH: 50
;   TYPE: DNA
;   ORGANISM: Homo sapiens
US-10-131-827-2866

  Query Match            70.9%;  Score 15.6;  DB 3;  Length 50;
  Best Local Similarity  81.8%;  Pred. No. 5.1e+02;
  Matches   18;  Conservative    0;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 ACAAAGCGCTTCTCTTTAGAGT 22
              | |||| |||| |||||||||
Db         45 ATAAAGTGCTTGGCTTTAGAGT 24
```

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Primary Examiner, Art Unit 1635
October 10, 2009